Bis(L-phenylalaninamidato)copper(II): Crystal Structure and Enantioselectivity

Rosangela Marchelli,*[a] Arnaldo Dossena,[a] Giuseppe Casnati,[a] Giovanna Gasparri Fava,[b] and Marisa Ferrari Belicchi[b]

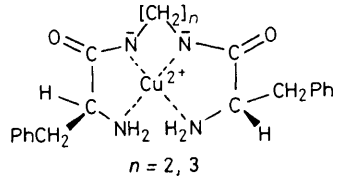
[a] *Istituto di Chimica Organica dell'Università, and* [b] *Istituto di Chimica Generale dell'Università e Centro di Studio per la Strutturistica Diffrattometrica del CNR, Via M. D'Azeglio 85, 43100 Parma, Italy*

Bis(L-phenylalaninamidato)copper(II) (**2**), whose crystal structure is reported, when added to the eluant, is able to perform chiral resolution of D,L-dansyl-amino acids in h.p.l.c. (reversed phase).

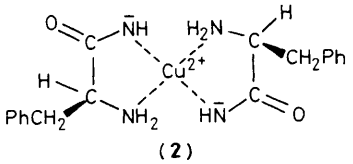
Copper(II) complexes of L-amino acids have been used as additives to the mobile phase for the chiral resolution of derivatized[1] or free[2] D,L-amino acids in h.p.l.c. (reversed phase). The mechanism of chiral recognition is still under discussion, although it is generally assumed to proceed *via* ligand exchange[3] and to involve the formation of diastereoisomeric ternary complexes.

In a general scheme aimed at studying the phenomenon of chiral resolution, we have recently reported[4] the resolution of D,L-dansyl-amino acids by copper(II) complexes with the tetradentate ligands *N,N'*-diphenylalanylethane- and *N,N'*-diphenylalanylpropanediamines (**1**).

We herein report the preparation and the crystal structure of the related analogous bis(L-phenylalaninamidato)copper(II) complex (**2**), and its enantioselectivity towards D,L-dansyl-amino acids in h.p.l.c. The present data may provide further clues to the mechanism of chiral recognition.



(**1**)



(**2**)

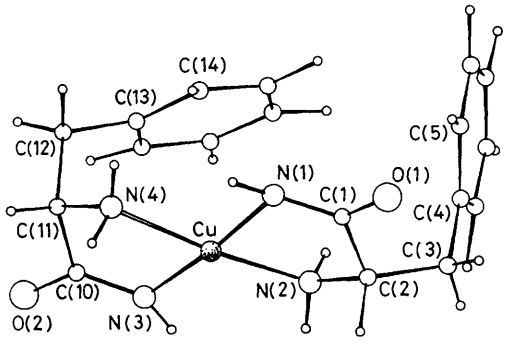


Figure 1. Molecular structure of bis(1-phenylalaninamidato)copper(II) (**2**). Important bond lengths (Å) and angles (°): Cu–N(2) 2.000(5), Cu–N(4) 2.011(5), Cu–N(1) 1.932(4), Cu–N(3) 1.943(4); N(3)–Cu–N(4) 82.4(2), N(1)–Cu–N(2) 82.3(2).

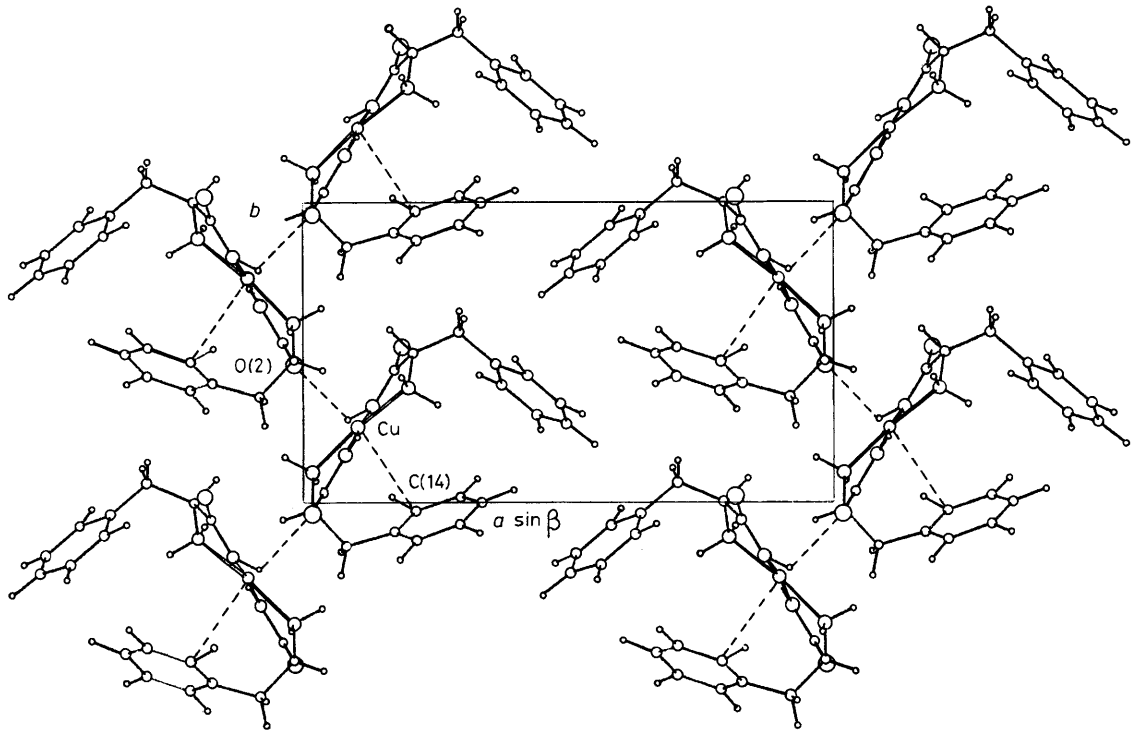


Figure 2. Crystal packing of complex (**2**) along [001].

Complex (**2**) was synthesized by treating L-phenylalaninamide hydrochloride (5 mmol) and copper acetate (2.5 mmol) in water with 1M NaOH to pH 11.6. Deep violet crystals (m.p. 215—218 °C, decomp.) were obtained in fair yield after 24 h at room temperature. Although bis(L-amino acidamidato)-copper(II) complexes are known in solution[5] and have been studied by potentiometry and spectroscopy, none has been isolated in the solid state so far.

The structure of complex (**2**), determined by *X*-ray crystallography,† is shown in Figure 1. The copper co-ordination is tetrahedrally distorted square planar and involves four nitrogen atoms from two phenylalaninamide molecules. The co-ordination is completed to give a very elongated square pyramid by a long interaction [2.732(5) Å] between copper and the O(2) carbonyl atom on an adjacent molecule. The copper ion is displaced 0.08 Å from the basal plane towards O(2). Therefore, infinite chains are formed around screw axes (Figure 2). The two phenylalaninamide residues are *trans* with respect to each other.

† *Crystal data:* $C_{18}H_{22}CuN_4O_2$, M = 389.9, monoclinic, space group $P2_1$, a = 15.963(2), b = 9.000(2), c = 6.041(2) Å, β = 91.09(3)°, U = 867.4(4) Å^3, Z = 2, D_c = 1.49 g cm^{-3}, D_m = 1.48 g cm^{-3}, $F(000)$ = 406, Cu-K_α radiation, λ = 1.54178 Å, μ(Cu-K_α) = 18.9 cm^{-1}; crystal size 0.42 × 0.14 × 0.07 mm^3. Data were measured to $2\theta_{max.}$ = 140°. A total of 1924 reflections were collected; of these 1565 had $I > 2\sigma(I)$ and were treated as observed and used in the subsequent analysis. No absorption correction was applied. The structure was solved by the heavy atom method and refined by full matrix least-squares to R = 0.0407 and R_w = 0.0543 (observed reflections only). The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

In contrast to bis(L-phenylalaninato)copper(II),[6] where both rings are extended outwards and away from the co-ordination sphere, in the present structure, as in (dimethyl sulphoxide)bis(L-phenylalaninato)copper(II),[7] one of the phenyl rings is approximately parallel to the basal plane of the metal co-ordination (Figure 1) and two carbon atoms are closer to Cu^{2+} [C(14): 3.173(7) and C(13): 3.314(5) Å]. Similar contacts were found in copper complexes with aromatic amino acids.[8—10]

The benzyl groups are on the same side of the co-ordination plane as has been found so far only in bis(*N*-Bz-L-Pro)Cu^{2+}.[9] The two five-membered chelate rings have different stereochemistry. The CuN(1)C(1)C(2)N(2) ring is in the *twist* conformation [puckering parameters: q_2 = 0.314(4) Å, ϕ_2 = −20.8(8)°, C_2 symmetry], and CuN(4)C(11)C(12)N(3) in the *envelope* conformation [puckering parameters: q_2 = 0.325(4) Å, ϕ_2 = 143.8(7)°, C_s symmetry].[11]

Bis(L-phenylalaninamidato)copper(II) (**2**), dissolved in the eluant (2 mM in water–acetonitrile), or prepared *in situ* at pH = 7.5 (as verified by potentiometric pH titration[12]) was used in h.p.l.c. (reversed phase C_{18}-column). Chiral resolution of D,L-dansyl-amino acids was obtained with α-values as high as 2.75. The D-enantiomers of the polar amino acids (glutamic and aspartic acid, serine, threonine) always elute before the L-, whereas for the apolar amino acids (valine, methionine, phenylalanine, tryptophan) the order of elution is reversed. It is noteworthy that the elution order observed with the related tetradentate analogues (**1**) is constant: the D-enantiomers always elute first. The present data indicate that different mechanisms are involved in the resolution process with the two systems. While with the bischelate complex (**2**) the chromatographic data are consistent with the ligand exchange mechanism, with the tetradentate complexes (**1**) chiral recognition may involve an initial outer sphere co-ordination.

This work was financially supported by M.P.I. (Ministero Pubblica Istruzione, Italy).

Received, 11th July 1985; Com. 990

References

1 E. Gil Av, A. Tishbee, and P. E. Hare, *J. Am. Chem. Soc.*, 1980, **102**, 5115; S. Lam, F. Chow, and A. Karmen, *J. Chromatogr.*, 1980, **199**, 295.
2 S. Weinstein, *Angew. Chem., Int. Ed. Engl.*, 1982, **21**, 218; *Angew. Chem. Suppl.*, 1982, 425.
3 V. A. Davankov, *Adv. Chromatogr.*, 1980, **18**, 139.
4 R. Marchelli, A. Dossena, G. Casnati, F. Dallavalle, and S. Weinstein, *Angew. Chem., Int. Ed. Engl.*, 1985, **24**, 336.
5 O. Yamauchi, H. Miyata, and A. Nakahara, *Bull. Chem. Soc. Jpn*, 1971, **44**, 2716; U. Gampp, H. Sigel, and A. D. Zuberbuhler, *Inorg. Chem.*, 1982, **21**, 1190.
6 D. Van der Helm, M. B. Lawson, and E. L. Enwall, *Acta Crystallogr., Sect. B*, 1971, **27**, 2411.
7 H. Muhonen and R. Hämäläinen, *Finn. Chem. Lett.*, 1983, 120.
8 D. Van der Helm and C. E. Tatsch, *Acta Crystallogr., Sect. B*, 1972, **28**, 2307.
9 G. G. Aleksandrov, Yu.T. Struchkov, A. A. Kurganov, S. V. Rogozhim, and V. A. Davankov, *J. Chem. Soc., Chem. Commun.*, 1972, 1328.
10 W. A. Franks and D. Van der Helm, *Acta Crystallogr., Sect. B*, 1970, **27**, 1299.
11 M. Nardelli, *Acta Crystallogr., Sect. C*, 1983, **39**, 1141, and references therein.
12 L. Barazzoni, R. Marchelli, A. Dossena, and G. Casnati, *J. Chromatogr.*, in preparation.